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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,745	06/22/2006	**Clifford David Jones**	101319-1 US	1031

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EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
1614	

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04/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,745	JONES ET AL.	
	Examiner	Art Unit	
	CRAIG RICCI	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10,11 and 15-19* is/are pending in the application.

4a) Of the above claim(s) *15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 11 and 19* is/are rejected.

7)☒ Claim(s) *8 and 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The amendments filed 12/12/2008 were entered.

Response to Arguments

2. Applicants' arguments, filed 12/12/2008, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Objections

3. Instant claims 8 and 10 are objected to as depending from a rejected claim.

Claim Rejections - 35 USC § 103

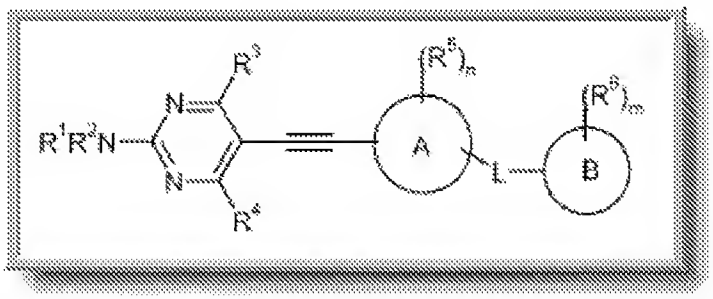
4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

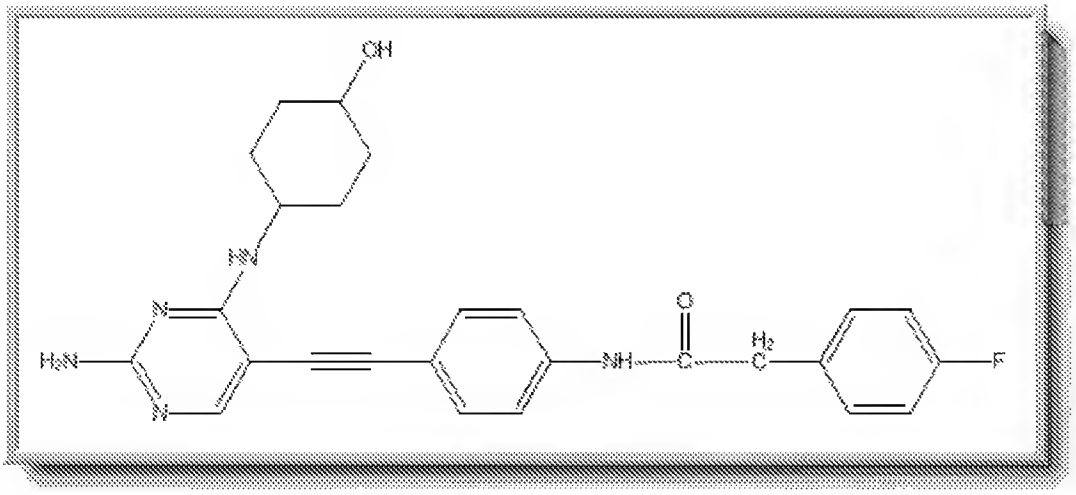
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

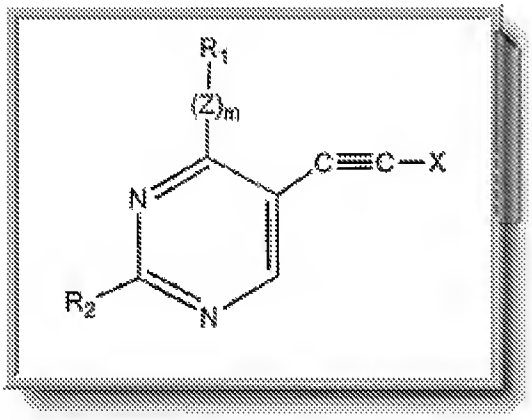
not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. **Claims 1-7, 11 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Beauchamp et al* (cited in a previous Action)**.

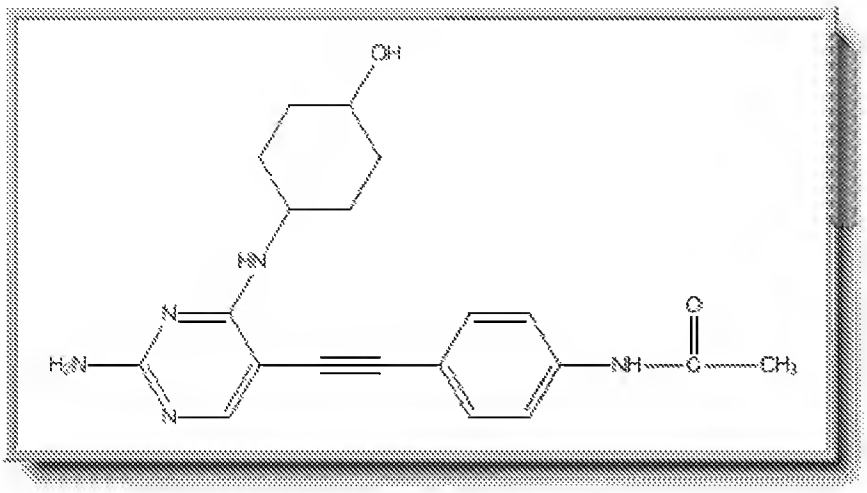
7. As discussed in a previous Action, instant claims 1-7, 11 and 19 are drawn to compounds of Formula I  and compositions which are disclosed as inhibitors of the Tie2 receptor tyrosine kinase, and which encompasses the following compound wherein R^1, R^2 and R^4 are hydrogen; R^3 represents the group NR^1R^2 wherein R^1 is hydrogen and R^2 is (3-6C)cycloalkyl$(CH_2)_x$ optionally substituted with hydroxy and, in which, x is 0; A is phenyl; n is 0; L is $-N(R^8)C(O)C(R^aR^b)$ wherein R^8, R^a and R^b are hydrogen; B is aryl (for example, phenyl); R^6 is halo (for example, fluoro); and m is 1:



8. *Beauchamp et al* teach compounds of Formula I



(Page 4, Lines 18-21) which are useful in the treatment of neurodegenerative disorders (Page 1, Line 4) and specifically disclose the following embodiment of Formula I



(Page 35, Example 31) wherein Z is NH and m is 0; R_1 is (C2-6alkyl)$_a$(C3-10cycloalkyl)$_b$(C1-6alkyl)$_c$ wherein a and c are 0 and b is 1, optionally substituted with hydroxy; R_2 is NH_2; X is C6-10aryl (specifically phenyl) optionally substituted with (y); and (y) is NH-CO-R_4 wherein R_4 is C1-12 alkyl (specifically CH_3). Accordingly, the only difference between the compound of Formula I recited by the instant claims 1-7, 11 and 19 and the compound taught by *Beauchamp et al* is that (in *Beauchamp et al*) R_4 is CH_3 whereas the instant application is drawn to a compound wherein the group corresponding to R_4 is (C1alkyl)aryl halogen. Significantly, *Beauchamp et al* teach only four possibilities for R_4; namely, H, C1-12alkyl, aryl or (C1-6alkyl)aryl halogen (Page 47, Lines 21-22). Thus, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to formulate the compound encompassed by instant claims 1-7, 11 and 19 in light of *Beauchamp et al* for the following reasons: **First**, *Beauchamp et al* specifically disclose a compound wherein X is phenyl substituted with NH-CO-R_4 and, furthermore, *Beauchamp et al* identify a finite and limited number of possibilities for R_4. A person of ordinary skill in the art at the time the invention was made would have pursued the finite

and limited number of possible groups with predictable and reasonable success to formulate the compound encompassed by instant claims 1-7, 11 and 19. **Second**, one of ordinary skill in the art would have recognized, in light of *Beauchamp et al* – which teach four possible variations at R_4 – that each possible group is functionally equivalent, and the simple substitution of one known element for another to obtain predictable results would be obvious.

9. Applicants, however, argue that *Beauchamp et al* only "partially" disclose compounds of the instant invention in that, for example, as to ring B of the instant compound, *Beachamp et al* do not teach a heteroaryl group or a heterocyclic ring as encompassed by the instant claims. Furthermore, Applicants note that, although *Beachamp et al* give rise to an equivalent of ring B in at least one instance (wherein R_4 is (C1alkyl)aryl halogen), this feature can be omitted. As such, Applicants contend that the contents of *Beauchamp et al* do not make the compounds of the present invention structurally obvious (Applicant Argument, Page 3). Although Applicant is correct that *Beauchamp et al* only partially disclose compounds encompassed by the instant claims, a **single** species taught by the prior art is sufficient to support a rejection over a claimed genus. As stated by the court in *In re Slayter*, 276 F.2d 408, 411 (CCPA 1960), "[a] generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus." Additionally, although it is also true that *Beachamp et al* do not **require** that R_4 is (C1alkyl)aryl halogen so as to provide an equivalent of instant ring B (i.e, R_4 can be CH_3 as in Example 31), it is clear that *Beachamp et al* teach that R_4 **can be** (C1alkyl)aryl halogen. Furthermore, as previously discussed, a person of

ordinary skill in the art at the time the invention was made would have pursued the finite and limited number of possible groups (including wherein R_4 is (C1alkyl)aryl halogen) with predictable and reasonable success. The skilled artisan would have recognized, in light of *Beauchamp et al* – which teach four possible variations at R_4 – that each possible group is functionally equivalent, and the simple substitution of one known element for another to obtain predictable results would be obvious. The fact that *Beauchamp et al* do not disclose a preference that R_4 is (C1alkyl)aryl halogen or provide examples wherein R_4 is (C1alkyl)aryl halogen would not have dissuaded the skilled artisan from formulating compounds wherein R_4 is (C1alkyl)aryl halogen under circumstances where *Beauchamp et al* teach only 4 possibilities at R_4.

10. Applicants further argue that it would not have been obvious to specifically modify R_4 in Example 31 (wherein R_4 is CH_3) to (C1alkyl)aryl halogen (as discussed above) in order to provide compounds which read on the instant claims. Applicants state that "since there is no suggestion to make the specific modification... the compounds of the instant invention are not obvious over *Beauchamp et al*" (Applicant Argument, Page 4, emphasis in original). Yet, as stated by the Court in *KSR International Co., v. Teleflex Inc.*, 127 US 1727 (2007), "the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim..." As discussed in the previous Action and reiterated above, *Beauchamp et al* specifically disclose a compound (Page 35, Example 31) differing from the instant compound in that R_4 (in *Beauchamp et al*) is CH_3 whereas the instant application is drawn to a compound wherein the group corresponding to R_4 is (C1alkyl)aryl halogen. Yet, as discussed,

Beauchamp et al teach only four possibilities for R_4; namely, H, C1-12alkyl, aryl or (C1-6alkyl)aryl halogen (Page 47, Lines 21-22). The skilled artisan would have recognized, in light of *Beauchamp et al* – which teach four possible variations at R_4 – that each possible group is functionally equivalent, and the simple substitution of one known element for another to obtain predictable results would have been obvious. Accordingly, a person of ordinary skill in the art at the time the invention was made would have pursued the finite and limited number of possible groups with predictable and reasonable success to formulate the compound encompassed by instant claims 1-7, 11 and 19.

11. Applicants additionally contend that the utility of the compounds should be taken into consideration as the utility of the compounds forms a part of that invention as a whole. This argument is not persuasive. The skilled artisan would have been motivated to make the above discussed changes to compound 31 taught by *Beauchamp et al* in an effort to synthesize functionally equivalent compounds with a reasonable expectation of success. Thus, while Applicant may be correct that the skilled artisan would not have made the modifications to *Beauchamp et al* in an effort to develop Tie2 inhibitors (or with any expectation that the modifications would lead to compounds having Tie2 inhibitory activity), the skilled artisan would still have made the modifications (resulting in a compound that reads on the instant claims) in an effort to synthesize compounds having NGF-like activity. Applicant is reminded that the instant claims are drawn to compounds and not to processes of using compounds as Tie2 inhibitors. Since the

compounds of the instant claims are *prima facie* obvious, the fact that the instantly claimed compounds may have activity as Tie2 inhibitors is irrelevant.

12. Instant claim 11 is drawn a pharmaceutical composition of Formula I in association with a pharmaceutically acceptable diluent or carrier. *Beauchamp et al* specifically teach "The formulations of the present invention comprise a compound of Formula I, as above defined... together with one or more pharmaceutically acceptable carriers therefor and optionally other therapeutic ingredients" (Page 14, Lines 23-24).

Conclusion

No new ground(s) of rejection are presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-

5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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